UNITED STATES OF AMERICA

FOOD AND DRUG ADMINISTRATION

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

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VACCINES AND RELATED BIOLOGICAL PRODUCTS

ADVISORY COMMITTEE

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MEETING ON PRESENTATION OF LABORATORY OF DNA VIRUSES,

DIVISION OF VIRAL PRODUCTS SITE VISIT REPORT

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MEETING BY TELECONFERENCE

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THURSDAY, MAY 6, 2004

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OPEN SESSION

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FOOD AND DRUG ADMINISTRATION
Rockville Pike
Building 29B, Conference Room C
Rockville, Maryland

1:30 p.m.

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COMMITTEE MEMBERS PRESENT:

GARY D. OVERTURF, M.D., Chair

MICHAEL D DECKER, M.D., Member

MONICA M. FARLEY, M.D., Member

RUTH A. KARRON, M.D., Member

PHILIP S. LARUSSA, M.D., Member
DAVID MARKOVITZ, M.D., Member

CINDY LYN PROVINCE, R.N., M.S.N., Member

RICHARD WHITLEY, M.D., Member

PETER PALESE, PH.D., Member

STEVEN SELF, PH.D., Member

WALTER ROYAL, III, M.D., Member

BONNIE M. WORD, M.D., Member

CBER STAFF PRESENT

CHRISTINE WALSH, R.N., Executive Secretary

DENISE ROYSTER, Committee Management Specialist

KATHRYN CARBONE, M.D., Acting Associate Director for Research

WILLIAM EGAN, PH.D., Acting Director, Office of Vaccines, Research, and Review

ANDREW LEWIS, PH.D., Chief, Laboratory of DNA Viruses, Division of Viral Products

I N D E X

P R O C E E D I N G S

1:36 p.m.

MS. WALSH: Good afternoon. I am Christine Walsh, the Executive Secretary for today's meeting of the Vaccines and Related Biological Products Advisory Committee. I would like to welcome all of you to the 99th Meeting of the Advisory Committee.

There's a speaker phone for public participation located here in Conference Room C of Building 29B on the NIH Campus.

This afternoon's session will consist of a presentation that is open to the public and a closed session as described in the Federal Register notice of April 19, 2004.

At this time I would like to introduce the Committee Members and ask that they acknowledge by saying present, if they can hear me.

The Committee Chair, Dr. Gary D. Overturf, Professor of Pediatrics and Pathology, University of New Mexico Medical Center.

DR. OVERTURF: Present.

MS. WALSH: Our consumer representative, Cindy Lyn Province, R.N., Associator Director of Bioethics Center of St. Louis.

MS. PROVINCE: Present.

MS. WALSH: Our non-voting industry representative, Dr. Michael D. Decker, Vice President, Scientific and medical Affairs, Aventis Pasteur.

DR. DECKER: Present.

MS. WALSH: Dr. Walter Royal III, Associate Professor of

Medicine, Morehouse School of Medicine.

DR. ROYAL: Present.

MS. WALSH: Dr. Monica M. Farley, Professor of Medicine, Emory University School of Medicine.

DR. FARLEY: Present.

MS. WALSH: Dr. Ruth A. Karron, Associate Professor, Division of International Health, Johns Hopkins School of Hygiene and Public Health.

DR. KARRON: Present.

MS. WALSH: Dr. Philip S. LaRussa, Professor of Clinical Pediatrics, Columbia University.

DR. LaRUSSA: Present.

MS. WALSH: Dr. Peter Palese, Chairman and Professor of Department of Microbiology, Mt. Sinai School of Medicine?

DR. PALESE: Present.

MS. WALSH: Dr. Bonnie M. Word, Assistant Professor of Pediatrics, Baylor College of Medicine, Texas Children's Hospital.

DR. WORD: Present.

MS. WALSH: Dr. Steven Self, Professor, Department of Biostatistics, University of Washington.

DR. SELF: Present.

MS. WALSH: Dr. David Markovitz, Professor, Division of Infectious Diseases, University of Michigan Medical Center.

DR. MARKOVITZ: Present.

MS. WALSH: Dr. Richard Whitley, Professor, Pediatrics,

Microbiology and Medicine, University of Alabama at Birmingham.

Dr. Whitley did tell me he may be joining us a little bit late today.

I would like to thank all Committee Members for taking time to join us today.

I would also like to make one announcement regarding a future VRBPAC meeting. There will be no meeting held on the reserved alternate dates of July 29th and 30th. After today's meeting, the next VRBPAC meeting is scheduled for September 22nd and 23rd, 2004.

Now I would like to introduce some FDA CBER Staff Members present at today's meeting and are currently seated in the room.

Dr. Kathryn Carbone, Acting Associate Director for Research; Dr. William Egan, Acting Director, Office of Vaccines, Research and Review; Dr. Andrew Lewis, Chief, Laboratory of DNA Viruses, Division of Viral Products, OVRR; and Denise Royster, Committee Management Specialist, VRBPAC Advisory Committee who worked very hard in making today's meeting a success. Thank you, Denise.

I ask that all our Committee Members identify themselves each time they speak. We have a transcriber present who will need your assistance in order to accurately transcribe all comments to the appropriate Committee Member.

I also ask our Committee Members do not use cellular phones since that can add extra unnecessary background to the line, noise to the line. Should during the teleconference a source of noise occur in your office, we would appreciate it if you

would use the mute button on your phone if you have that option. We ask that you do not place us on hold because many clinical centers have background music that can be very distracting to those remaining on the teleconference line.

I would now like to read into public record the conflict of interest statement for this meeting.

The following announcement addresses conflict of interest issues associated with today's meeting of the Vaccines and Related Biological Products Advisory Committee on May 6th related to the review and discussion of the intramural research programs of the Laboratory of DNA viruses, Division of Viral Products. Based on the agenda made available, it has been determined that the Committee discussions present no potential for a conflict of interest.

That ends the reading of the conflict of interest statement.

Dr. Overturf, I turn the meeting over to you.

DR. OVERTURF: Thank you. This is Dr. Overturf and I'd like to welcome the Members of the Committee to this meeting. The purpose of this meeting is to review the site visit report of the Laboratory of DNA Viruses which is in the Division of Viral Products in the Office of Vaccines, Research and Review.

You should have all received prior to this time either by e-mail or by direct mail the prior documents which include, among other things, the site report visit itself which is a document in which the chair of the Committee, Dr. Walter Royal is listed at the

top of the page.

The first speaker today will be Dr. Andrew Lewis from the FDA and I will turn the meeting at this time over to Dr. Lewis.

DR. LEWIS: Thank you, Dr. Overturf. I'm Andrew Lewis, Chief of the Laboratory in DNA Viruses, Division of Viral Products.

It's my job today to present the Committee with a brief summary of the Laboratory of DNA Viruses in preparation for your discussion of our site visit. The Laboratory of DNA Viruses is an organizational unit within the Division of Viral Products. The mission of our laboratory is basically fourfold. First, we evaluate and regulate vaccines and other products involving DNA viruses, including pox viruses, herpes viruses, adenoviruses, and paplomaviruses.

Second, we review and provide consultations to other CBER offices on submissions using DNA viruses as recombinant gene delivery systems.

Third, we evaluate and provide consultations on issues related to cell substrates and adventitious agents.

And last, but not least, we strive to maintain DDP in CBER's intellectual base by doing research on DNA viruses and cell substrates.

I would like to point out to the Committee that managing these responsibilities requires constant attention of a laboratory staff with regard to the use of the limited time and resources that are available. In looking back over the past several years, I feel

quite good about the way our staff has performed in managing its resources.

The Laboratory of DNA Viruses was established in 1988 and it is composed of four research teams. These teams include the Unit on Cell Substrates headed by myself with a staff of four; the Unit on DNA Virusing Expressing headed by Jerry Weir with a staff of three; the Unit on Pox Virus Biology headed by Mike Merchlinsky with a staff of six; the Unit of Viral Latency headed by Phil Krause, also with a staff of six.

More details about each of these units are provided in their site visit book which I believe each of you has a copy of.

Concerning the staff of the Laboratory, I should also point out that in 2000, Jerry Weir was appointed Director of the Division of Viral Products and later that same year, Phil Krause, from the Latency Unit, was appointed the Deputy Director of the Division of Viral Products.

The principal regulatory responsibilities of our laboratory include the review of investigational new drug applications and biologics license applications for DNA virus products. The laboratory is a unit within the Division of Viral Products in the Office of Vaccines with the prime responsibility for reviewing, licensing and managing post-licensure issues associated with chicken pox and smallpox vaccines.

The laboratory is also responsible for the evaluation of plasma infectors, uses vaccines for DNA virus in new diseases and we

share the responsibility for evaluation of DNA viruses used for gene therapy.

In addition, the laboratory evaluates and advises on cell substrate and adventitious agent issues within the Office.

The laboratory is involved with all aspects or the regulation of products involving DNA viruses as well as cell substrates used for the manufacture of viral vaccines. Our regulatory responsibilities encompass all phases of product development from pre-IND guidance, IND submissions, product license application and supplements, post-marketing commitments and vaccine lot release.

The review workload handled by the laboratory over the period covered by the present site visit has increased significantly. In 1997, the laboratory was responsible for the review of 178 INDs. These included original submissions as well as amendments and in 2003, the laboratory reviewed 246 INDs, 12 biologic license application supplements and released 342 lots of combined chicken pox and smallpox vaccines.

The laboratory typically receives and reviews approximately 10 original submissions each year and 250 to 300 supplements.

In addition to the user regulatory work, our laboratory is also involved in numerous other activities that are an integral part of our regulatory mission. These activities include organizing and participating in discussions with you as our Advisory Committee;

inspecting vaccine manufacturing facilities; developing regulatory guidance documents; serving as FDA experts to international bodies such as the World Health Organization; and organizing international workshops.

The program report provided by each laboratory unit in the site visit book contains much more information about these activities.

The research programs in the laboratory are designed to complement and support our regulatory mission by focusing on issues that we believe to be critical to the evaluation, development and safety of the products related to DNA viruses and by investigating the basic mechanisms of biology and pathogenesis of the viruses and products we regulate. To give you a very brief look at some of our research projects, the Unit on Cell Substrates is developing an assay or attempting to develop an assay to assess the potential risk of the oncogenic activity of DNA from continuous cell lines and has evaluated concerns about the ability of VERO cells to evolve from non-tumorgenic to tumorgenic phenotypes by tissue culture passage. The Unit of Viral Gene Expression and the Unit on Pox Virus Biologies are collaborating to develop data regarding protected immunity, new generation of smallpox vaccines and to determine the relative importance of different aspects of the immune response to smallpox vaccines. One or more of these responses might be possible surrogates that can be used to evaluate the efficacy of new smallpox vaccines.

In addition to its on-going work, the mechanisms of viral latency, the Unit on Latency is developing nonspecific methods to detect adventitious agents which include the use of nanovirus sensors for virus detection as well as degenerate PCR mechanisms.

To support these research activities, the four units of the laboratory brought in over $700,000 to CBER in 2003 and I think I can be frank by saying that without these funds, it would not have been possible for us to maintain our research programs at their current levels.

Some of the major things that we've accomplished over the past five years include the re-licensure of the Smallpox Vaccine Drive Acts, receiving a patent for the in vitro ligation of foreign DNA in large eucaryotic vectors, identifying sequence differences between vaccine strain and wild type chicken pox viruses, identifying virus reactivation as a potential for persistent immunity in chicken pox vaccinees, organizing and publishing the proceedings of an international workshop on cell substrates in 1999, stimulating work on SV-40 as a potential human polymer virus by developing small working groups and funding small projects at other institutions.

I think this sort of concludes my summary of the laboratory's activities. I would like at this time to express our appreciation to those Members of the Committee and to the Committee itself for participating in this review and commenting on our progress.

Thank you very much.

DR. OVERTURF: Thank you very much, Dr. Lewis. Before we proceed, we need to request from the FDA whether there have been members of the public or others who wish to speak in the Open Public Hearing.

MS. WALSH: I see no one in the room right now, Dr. Overturf.

DR. OVERTURF: Okay, with that, we can dispense with the statement on the Open Public Hearing. And we can proceed with the rest of the session and the next speaker is Dr. Walter Royal, who will present the results of the site visit report.

DR. ROYAL: Thank you, Dr. Overturf --

MS. WALSH: Excuse me, excuse, this is Christine for one second. Can we just hold up for one second?

DR. OVERTURF: Before we go to closed session?

MS. WALSH: Yes, before we go into closed session.

DR. OVERTURF: that would be fine.

MS. WALSH: With the report from Dr. Royal, we'll be moving into a closed session. So anyone that would need to leave right now -- and before we do that, any questions for Dr. Lewis before he leaves, from the Committee?

DR. OVERTURF: Are there any questions for Dr. Lewis?

DR. LEWIS: Thank you.

MS. WALSH: Thank you, Dr. Lewis. And prior to that, we'll just go into closed session now.

(Whereupon at 1:52 p.m., the open session was concluded.)